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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,877	DECRISTOFARO ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,9-14 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,9-14 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

Applicant's election with traverse of Group II, claims 5-14, 30 and 33 in the reply filed on 6/21/04 is acknowledged. The traversal is on the ground(s) that other sequences are "reasonably related" to elected SEQ ID NO's 53 and 54, therefore there would not be an undue burden on the examiner to search for all of SEQ ID NO's 43-54. This is not found persuasive because as disclosed on at least pages 123-137of the specification, SEQ ID NO's 43-49 and 51 encode proteins which are different in sequence from the protein (SEQ ID NO: 54) encoded by SEQ ID NO: 53. While the encoded proteins do have some regions which align with each other, they are still different sequences, and thus may have different properties, expression patterns, tissue specificity, etc. Similarly, the nucleic acids represented by SEQ ID NO's 43-48 are different sequences, and are therefore distinct. In addition, each nucleic acid sequence may have different transcriptional and translation patterns, may be linked to, and thus controlled by different regulatory regions, etc. It is noted that while applicant argues that the sequences are "reasonably related," applicant has NOT admitted that the sequences are obvious over one another or lack patentable distinction.

Each different sequence requires its own separate search and consideration. It is noted that each sequence may further require a different search and consideration with regard to utility and enablement issues. In addition, a search for any single sequence requires a search of nonpatent literature and foreign patents in addition to a search of US patents and publications. For these reasons, the examiner maintains that the sequences represented by SEQ ID NO's 43-52 are separate and distinct from SEQ

ID N O's 53 and 54, and maintains that it would be burdensome to search and examine more than the elected sequences.

The requirement is still deemed proper and is therefore made FINAL.

An action on the merits of elected, pending claims 5, 9-14 and 30 follows.

Priority

The priority statement on the first page of the specification recites improper terminology. The sentence should state that --benefit of-- priority applications is claimed instead of "priority to" those applications. Appropriate correction is requested.

Information Disclosure Statement

The IDS's filed 5/2/02 and 4/8/03 have been considered in full.

Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 5, 9-14 and 30 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial,

and credible utility or, in the alternative, a well-established utility. See MPEP 2107 for a discussion of "specific, "substantial, and credible" utility.

The claimed subject matter is not supported by a specific, substantial, and credible utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. The examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter.

The specification discloses on pages 8 and 139-148 that SEQ ID NO: 53 encodes SEQ ID NO: 54, which is homologous to a rat MEGF6 (murine EGF) protein. Page 148 discloses that NOV15 proteins comprise EGF domains. The specification further discloses on pages 13 and 149-150 that based on homology to MEGF, all the proteins designated NOV15 (including elected SEQ ID NO: 54) may be used to treat a recited "laundry list" of disorders, which list encompasses neurological , immunological, pulmonary, cardiac, and nephritic disorders and diseases. According to the disclosure, the members of NOV15 may also be used to treat behavioral disorders and disorders for which the etiology is unknown (e.g. anxiety, addiction, pain). No correlation is made between particular disorders, or classes of disorders, and either of SEQ ID NO: 53 or 54. The specification further discloses, on page 150, that NOV15 proteins may be used to detect specific cell types, but fails to disclose a correlation between any particular cell type or types and individual SEQ ID NO's. Pages 503-521 of the specification disclose results of expression assays for NOV15 proteins; however, the specification does not

disclose whether any of the probes is specific for SEQ ID NO: 53 (see pp. 503-504) and all of the results are directed to expression of SEQ ID NO: 45 (pp. 517-519). It is noted that these results are quite different from those of SEQ ID NO: 43 (p. 503), which also a NOV15 protein. Further, there is no clear pattern of tissue expression, developmental expression, or correlation with disease tissue. SEQ ID NO: 45 is found in a plethora of tissues and at moderate levels in both normal and cancer cells. Again, it is noted that no results specific to SEQ ID NO: 53 are disclosed. Thus, a utility to treat, detect, screen for, prognosticate, diagnose, etc. a disease or disorder is not a specific, substantial and credible utility for SEQ ID NO's 53 and 54. Likewise, a utility to perform tissue typing or pharmacogenomics based on expression of SEQ ID NO: 53 or 54 is not a specific, substantial and credible utility for SEQ ID NO's 53 and 53.

Identification as a member of a class of proteins or nucleic acids may impart utility to a sequence when every member of the class has a specific, substantial and credible utility, such that one skilled in the art would be apprised of the utility of every member of the class merely by the identification. Such is not the case for proteins comprising EGF domains. The class of "EGF" proteins is large and has many subclasses wherein each subclass has a separate set of functions. In some cases, the subclasses are defined merely by structure and the actual function, or putative utility, has not yet been elucidated. The specification discloses, on page 149, that there are at least three different types of MEGF proteins, each with its own function and expression pattern (time and tissue). Within the family of MEGF proteins, the prior art teaches that there are at least four subclasses, as taught by NAKAYAMA et al. (Genomics (1998)

vol. 51, pp. 27-34). While NAKAYAMA teaches that these EGF proteins are known to be "biologically important", he also teaches that each protein has a different and distinct utility and that the different proteins correlate to different disorders (p. 27). For example, MEGF1 appears to play a role in the cerebellum (p. 29) while MEGF 4 and 5 are homologous to proteins critical in formation of axon tracts and MEGF5, at least, is not expressed in cerebellum (p. 31). MEGF8 is most similar to the LDL-receptor family (p. 38) and thus would be expected to have a completely different expression pattern and disease correlation than any of MEGF1, 4, or 5. Within the subclass of "Notch" proteins, there are different functions and thus different putative utilities. IRVIN (IDS Ref: J. Compar. Nuerol. (2001) vol. 435, pp. 167-181) discloses that Notch receptors have different expression patterns and play multiple roles in CNS development (p. 180). Thus, any given subclass of EGF-type proteins may comprise multiple functions, expression patterns, and correspondence to different diseases or disorders. Because the families comprise many members with different or unknown utilities, as set forth above, identification of a protein as an "EGF" protein, or even as belonging to the MEGF family, does not impute utility to the protein so identified. Thus, identification of SEQ ID NO: 54 as one homologous to MEGF does not impute a specific, substantial and credible utility to either SEQ ID NO: 53 or 54.

Pages 4-6 and p. 365 et seq. set forth myriad uses for the inventive sequences, including gene therapy, treatment, diagnosis, or detection of disease (with a long list of diseases set forth on page 4), chromosome mapping, tissue typing, tissue regeneration, generation of antibodies, and use as a research tool. As set forth above, SEQ ID NO's

53 and 54 are not known or disclosed to be correlated to any disease or disorder, therefore uses for treatment, including gene therapy, diagnosis or detection are not specific, substantial and credible utilities. There is no disclosure anywhere that SEQ ID NO: 53 or SEQ ID NO: 54 is involved in tissue regeneration or is known to be expressed during axonal outgrowth, bone formation, cellular dedifferentiation, etc. as would be expected for a sequence involved in tissue regeneration, therefore this is not a specific, substantial and credible utility for SEQ ID NO's 53 and 54. The instant specification does not disclose whether SEQ ID NO: 53 is differentially expressed in a particular tissue type or a particular stage of development, such that SEQ ID NO: 53 or 54 can be used for tissue typing, therefore tissue typing is not a specific, substantial and credible utility for SEQ ID NO's 53 and 54. Uses of chromosome mapping, generation of antibodies and as a "research tool" are generic to the classes of nucleic acids and proteins, and are therefore not specific, substantial and credible with regard to SEQ ID NO's 53 and 54. Further, with regard to use as a research tool, applicant is reminded that a use to do further research is not a proper utility under 35 USC 101.

Neither the prior art nor the instant specification disclose a "well-known utility" for either SEQ ID NO: 53 or SEQID NO: 54, nor does the instant specification set forth a specific, substantial and credible utility, as set forth above, therefore the claims lack utility.

Applicant should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

Claims 5, 9-14 and 30 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a LACK OF ENABLEMENT rejection.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

One skilled in the art would not know how to use a pharmaceutical composition comprising a nucleic acid which encodes SEQ ID NO: 54 because neither the specification nor the prior art teach how to do so. The claim is directed to a composition comprising a pharmaceutically acceptable carrier and a nucleic acid and therefore

encompasses pharmaceutical compositions (i.e. for administration). While it is well-known in the art how to make and administer a composition comprising a nucleic acid and a pharmaceutically acceptable carrier, and the specification discloses how to do so on pages 361-364, one skilled in the art would not know how to USE the invention; i.e. what to treat, with the inventive composition. As set forth above, the instant specification discloses "laundry lists" of diseases for treatments, but does not disclose, which, if any, are to be treated with a composition comprising SEQ ID NO: 53. The state of the prior art is such that it is known that a few, but not all, MEGF proteins are known to be correlated with a disease (see NAKAYAMA, supra, p. 31, Table 1). Also as set forth above, SEQ ID NO: 53 is not know or disclosed as being correlated or associated with a particular disease, disorder, tissue type, developmental stage, etc., such that one skilled in the art would know what to treat with the composition claimed. The level of skill in the art is acknowledged to be high; however, as the skilled practitioner would have to guess at the disease or disorder for which the composition is to be administered, the skilled practitioner would also have to guess at mode of treatment, dosage, formulation, etc. This represents undue experimentation. As one skilled in art would not know how to use the claimed composition for the reasons set forth above, claim 30 is not enabled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 limits a nucleic acid to one which hybridizes under "stringent conditions" to a claimed nucleotide. Page 319 of the specification sets forth some conditions identified as "stringent", but also specifically discloses that this is a "non-limiting" example. As it is therefore unclear what applicant intends for "stringent" hybridization conditions, one skilled in the art would not be apprised of the metes and bounds of the invention, and the claim is indefinite. Applicant is reminded that limitations of the specification can not be read into the claims.

Claim 11 recites the term "complement" in line 1. This term may have many meanings in the art; e.g. a sequence which is fully complementary to another, one which is partially complementary to another, one with a particular degree of identity, etc. As it is unclear what meaning applicant intends for the term "complement", the claim is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by NAKAYAMA et al. (IDS ref: NCBI accession number AB011532, 8/22/1998), as supported by MEINKOTH et al. (Analytical Biochem. (1984) vol. 138, pp. 267-284).

NAKAYAMA teaches a sequence which is 63% identical to SEQ ID NO: 53 over a duplex length of 5523 base pairs comprising 966 mismatches. Using the equation set forth on page 269 of MEINKOTH, and using the conditions set forth on page 319 of the instant specification:

% GC is estimated to be 50%. % mismatch = 17.5 (MEINKOTH teaches that for sequences over 150 bp, 1°C is subtracted for every 1% mismatch);
At 6X SSC, the T_m=83.7°C and at 0.2X SSC, T_m=59.1°C, therefore NAKAYAMA's sequence would be expected to hybridize under stringent conditions to SEQ ID NO: 53, and claim 10 is anticipated.

NAKAYAMA discloses both a gene and mRNA comprising his sequence. Genomic DNA is double-stranded, therefore a teaching for one strand is inherently a teaching for its complement. As one strand of NAKAYAMA's sequence is at least partly complementary to SEQ ID NO: 53, claim 11 is anticipated.

Conclusion

Claims 5, 9-14 and 30 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571)

272-0720. The examiner can normally be reached on Mon. to Wed, 7:30-4; Thurs 7:30-6; Fri 7-1 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
9/4/04